PROGRESS REPORT 7:

"CORTICAL CONTROL OF NEUROPROSTHESES"

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THIS QPR IS BEING SENT TO YOU BEFORE IT HAS BEEN REVIEWED BY THE STAFF OF THE NEURAL PROSTHESIS PROGRAM.

This progress report covers: 1- revision of a manuscript detailing our progress on showing feasibility of robot arm control from neuronal population recordings in rats. 2- revision of a manuscript detailing our progress in the chronic recording of large ensembles of neurons from the somatosensory and motor cortices of monkeys trained in an arm movement task. 3- recent findings that motor cortical population activity encodes timing and magnitude of limb movement over a characteristic time range, 4- efforts to record neuronal populations in monkeys which have been trained using 3D limb movement tracking and tactile virtual reality instrumentation, 5- continuing efforts to finish a computer based real-time interface for neurorobotic applications.

1- Revision of a manuscript detailing our progress on showing feasibility of robot arm control from neuronal population recordings in rats.

A manuscript, entitled "**Direct real-time control of a robot arm using signals derived from neuronal population recordings in motor cortex**", by John K. Chapin, et al., is now under revision. The following is the abstract of the submitted paper, as currently revised:

To investigate the feasibility of using brain activity for robotic control, up to 46 neurons were simultaneously recorded in the forelimb motor cortex, ventrolateral thalamus and/or cerebellum of rats initially trained to obtain water by depressing a lever to control movement of a robot arm. Neuronal population activity peaked just before onset of lever movement, but this peak encoded the trajectory of movement over the next 3-500 ms. Further transformations of this population activity yielded output functions that closely matched the timing, magnitude and direction of forelimb movements. After training, the control of the robot arm was switched from the lever press to the neuronal population. Animals with at least 25 recorded neurons successfully used this population signal to move the robot to the water source and return it to their mouths. Over continued training in this "neurorobotic" mode, the brain activity became dissociated from actual movement, whose magnitude diminished over time. Such neuronal population signals might therefore be useful for controlling prosthetic devices.

2- - Preparation and submission of a manuscript detailing our progress in the chronic recording of large ensembles of neurons from the somatosensory and motor cortices of monkeys trained in an arm movement task.

A manuscript entitled, **"Simultaneous representation of tactile information by distinct primate cortical areas rely on different encoding strategies"**, by Miguel A.L. Nicolelis, et al., is under revision. The following is its abstract:

Simultaneous multisite neural ensemble recordings were carried out to investigate the single trial representation of tactile information in the infragranular layers of three distinct areas of the primate somatosensory cortex (areas 3b, SII, and 2). As a rule, individual cortical neurons in these areas exhibited broadly tuned sensory responses which could not be used to identify the location of the stimulus on a single trial basis. Despite this lack of specificity at the single neuron level, the precise location of tactile stimuli could be reliably predicted on a single trial basis by considering the spatiotemporal firing patterns of small neural ensembles (30-40 neurons) from each of these three cortical areas. Latency analysis indicated that such a single-trial discrimination can be achieved simultaneously by small ensembles in all three cortical areas. Moreover, manipulations of the population spike trains suggested that each of these cortical areas might employ different encoding strategies, that include both a firing rate and a temporal code, to unambiguously represent the location of a tactile stimulus. These results support the notion that ensembles of broadly tuned neurons, located in both primary and higher cortical fields, can have access to unequivocal information pertinent to the location of a tactile stimulus almost concurrently and on a single trial basis.

2- Recent findings that motor cortical population activity encodes timing and magnitude of limb movement over a characteristic time range

Further analysis of neuronal population responses in six animals during repeated bar pressing movements revealed a consistent phenomenon wherein the peak of neural activity just preceding the onset of bar movement was highly correlated with the timing and magnitude of movement over the subsequent 500 ms. Time-shifted cross-correlation studies revealed that normal fluctuations in the amplitude of the pre-movement neuronal population activity peaks were highly correlated with concomitant variations in the magnitude of bar press movements over the subsequent 500 ms in the same trials. Thus, in trials where the pre-movement neural activity was high, the bar movement was sufficient to position the robot arm under the water dropper within 500 ms. In trials where the pre-movement activity was low, the initial pressing movement was insufficient, requiring the animals to initiate a supplemental movement to finally obtain the water. The correlation matrices of these data show that the pre-movement peak accurately predicted the timing and magnitude of movement over the first 500 ms of bar movement, but not these supplemental movements. These were better correlated with smaller peaks in cortical activity occurring from 300-600 ms following initial onset of bar pressing. In general, cortical activity was uncorrelated or negatively correlated with movement occurring at the same time. Similarly high correlation coefficients were found across the six animals (mean R_{max} = .69) between the pre-movement cortical peaks and movement magnitudes in the period from 300-600 ms post-movement-onset. Within the same time comparisons, neuronal populations in the VL thalamus and cerebellum were signficantly, but more weakly correlated with movement (R= .44 and .34 respectively). EMG recordings (obtained in two animals) demonstrated that such motor cortical encoding of movement was tightly related to a similar encoding of magnitude of bursts of EMG activity (mean R_{max} = .74) in the triceps and wrist extensor muscles beginning 50-100 ms after the cortical peak, and continuing for 100-300 ms. Thus, by prospectively encoding the timing and magnitude of muscular force bursts directed against a spring load, these neurons predicted the trajectories of the forelimb movements 200-500 ms hence. The above findings thus provide evidence that the motor cortex, VL thalamus and cerebellum can all provide information usable for encoding of movement trajectories. They also demonstrate the necessity of using neuronal populations rather than single neurons.

4- Successful implementation of 3D limb movement tracking and tactile virtual reality instrumentation in the monkey,

As previously reported, Drs. Nicolelis and Brisben, at Duke University, have successfully trained monkeys in the paradigm which uses external "virtual reality" devices to control limb movement. Unfortunately, the first such animal died shortly after the surgery in which 64 neurons were implantated in four sensorimotor cortical areas. The death was apparently unrelated to the implants. Now, another animal has been successfully implanted with 64 microelectrodes in the sensorimotor cortex. Soon it will be ready for experimentation.

5- Continuing efforts to finish a computer based real-time interface for neurorobotic applications.

Plexon Inc. has delivered its Windows NT version of their multi-neuron acquisition software/hardware system. This allows simultaneous execution of multiple tasks, employing the internal client-server features in the new NT OS. This will involve setting up a data server to monitor the on-line discrimination of brain neurons, and feed this information in real-time to multiple clients, including on-line analysis applications, on-line statistical or neural network applications, and from there to on-line robotic control applications. Even though Windows NT is not a true real-time OS, it should work well within the time constraints in this application.

Beyond this, Plexon has now hired a new programmer who will be spending full time on this project. He has been assigned to work on a computer real-time interface which will be faster and more efficient than the system described above. Rather than using the client-server features of NT OS, it will work within the Plexon data acquisition kernel to directly weight and integrate multineuron recordings in real-time. This software segment will then output the integrated neuronal population signal through a digital output port to directly control a torque motor device attached to a "robot arm". This device will therefore implement in computer software the equivalent of the hardware device that the PI has already used for such a purpose. This is advantageous in that it should provide a quick solution to both the Philadelphia and Duke labs that are carrying out these experiments. Also, since it is faster, it gets us closer to the ultimate technology that will be used for these neuroprosthetic devices. The drawback for now is that it will not allow easy implementation of the elaborate mathematical transformations that we have been investigating. Fortunately, the NT OS client server system should allow such transformations to be easily implemented. The combination of both approaches should provide the laboratory investigators maximal flexibility in their experimentation with different schemes for transforming the cortical signals to motion system (of FNS) outputs.